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EXAMINER	
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ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
01/11/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	09/772,445	KLEINMAN ET AL.	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *187-223* is/are pending in the application.

4a) Of the above claim(s) *189,190,197,201,206,207,214,218 and 222* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *187,188,191-196,198-200,202-205,208-213,215-217,219-221 and 223* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/28/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendments and arguments filed 11/18/10 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Previously, applicant elected group 1 (claims 1-40,47-49,53-61,133-136) (11/5/04) and elected a species comprising amino acids LKKTET (2/24/05) for the would healing polypeptide. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Due to the addition of new claims an additional election of species requirement was sent 1/6/09.

Applicant's election of the following species:

Patient population: skin wound

Further agent: transforming growth factor beta

Further excipient: sterile water

in the reply filed on 2/5/09 is acknowledged.

In the instant case, each of the elected species were found in the prior art. In particular the peptide thymosin beta 4 comprises LKKTET (compare claim 188). Any art that was found in the course of searching for the elected species that reads on non-elected species is also cited herein. In accord with section 803.02 of the MPEP the Markush-type claims and the claims to the elected species are rejected and claims to the nonelected species are held withdrawn from

consideration. In accord with section 803.02 of the MPEP the search is not extended unnecessarily to cover all species (such as all isoforms).

Claims 1-186,224-236 have been cancelled.

Claims 189-190,206-207 are to a species other than thymosin beta 4 (i.e. an LKKTET containing peptide), claims 197,201,214,218 are to a species of further agent other than transforming growth factor beta, claim 222 is to a patient population other than skin wound.

Claims 189-190,197,201,206-207,214,218,222 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2/5/09.

Claims 187-188,191-196,198-200,202-205,208-213,215-217,219-221,223 are under consideration.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 7/28/10 has been considered by the examiner.

Priority

A section entitled 'priority' appeared in previous office action. Based on the claim amendments the section has been updated.

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or

more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See Transco Products, Inc. v. Performance Contracting, Inc., 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/094,690 (7/30/98), fails to provide adequate written description in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

In the instant case, Claims 187,191-196,198-200,202-204,208-213,215-217,219-221,223 refer to the amino acid sequence LKKTET or to isoforms.

Lack of Ipsis Verbis Support

Application No. 60/094,690 (7/30/98), is void of support for the amino acid sequence LKKTET or for isoforms.

Lack of Implicit or Inherent Support

Section 2163 of the MPEP states: 'While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure'.

Although the above statement is with respect to new claim limitations, the analysis is similar in determining conditions for receiving the benefit of an earlier filing date.

Application No. 60/094,690 (7/30/98), does recite thymosin beta 4. However, the disclosure of thymosin beta 4 would not lead one to the sequence LKKTET or to isoforms. For at least these reasons, one would not conclude that Application No. 60/094,690 provides adequate support for Claims 187,191-196,198-200,202-204,208-213,215-217,219-221,223.

Claim Rejections - 35 USC § 102

Claims were previously rejected based on Turischev (Farmatsiya 'Examining the effects of thymosin on the healing of flat cutaneous wounds in rats' v45 (1996) pages 42-43; first cited 12/30/09) as evidenced by Mann (US 6,030,948). Since the claims have been amended the rejection is updated to correspond to the instant claims.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 187-188,192-193,195-196,200,202-205,209-210,212-213,217,219-221,223 are rejected under 35 U.S.C. 102(b) as being anticipated by Turischev (Farmatsiya 'Examining the effects of thymosin on the healing of flat cutaneous wounds in rats' v45 (1996) pages 42-43; first cited 12/30/09) as evidenced by Mann (US 6,030,948).

It is noted that Turischev is in a non-English language. A translated version of the article has been provided and will be relied upon and referenced to herein (Turischev translation of

Farmatsiya 'Examining the effects of thymosin on the healing of flat cutaneous wounds in rats' total of 7 pages including the cover page)

Turischev teach the effect of thymosin on the healing of flat skin wounds in rats (title). Turischev teach that Thymosin (5^{th} fraction) was used in the experiments (page 1 last paragraph). Turischev teach that the composition was administered intraperitoneally or topically to rats with wounds (page 2). Turischev teach that there is clear acceleration of the healing rates and that a dose of 0.8 ug accelerated wound healing (page 3). Turischev does not recite the components of thymosin 5^{th} fraction. Mann teach (column 4 lines 8-53) that thymosin fraction 5 contains thymosin beta4 (column 4 line 31) and thymosin alpha 1 (column 4 line 26). Mann is cited as a universal fact to reveal the components of thymosin fraction 5 and thus need not be prior art (MPEP 2124).

Since Turischev teach rats with skin wounds the patient population of claims 187,202,203 (i.e. skin damage),204,219,220 (i.e. epidermal),221,223 (skin damage) are met. Since Turischev teach that the composition was administered intraperitoneally or topically via a solution (page 2) the limitations of claims 192-193,195,196,209,210,212,213 are met. Turischev teach that Thymosin (5^{th} fraction) was used in the experiments (page 1 last paragraph) and Mann states that such fraction contains thymosin beta 4 and thymosin alpha 1 (see applicants original claim 12 and admission on page 21 lines 4-5 of the reply dated 3/30/10, and see page 11 of specification of the current invention) the composition limitations of claims 187,188,200,204,205,217 are met.

It is noted that certain claims recite properties – actin-sequestering activity, stimulates epithelial migration, etc. Since Turischev teach the elected agent (i.e. thymosin beta 4) which is recited in the claims (claim 188 for example) the claim limitations are met (see also MPEP

2112.01). It is noted that the claims refer to effective amounts. Since Turischev expressly states (page 3) 'this is evidence of a clear acceleration of the healing rates' and 'a dose of 0.8 ug accelerated wound healing' the amounts are effective.

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting regeneration (claim 187) do not result in a manipulative difference and do not serve to limit the claims.

It is noted that claim 187 and claim 204 recite 'consisting essentially of'. First, it is noted that the claims also recite the open language 'containing' and claims 198,210,212,215,217 are evidence that there can be other components in the mixture. Further, MPEP 2111.03 states: 'For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising."'. In the instant case the specification provides no specific information of the basic and novel characteristics thus the term is construed as equivalent to comprising.

Response to Arguments 102

Applicants argue (pages 8-9) that the claims recite wound repair and regeneration which refer to new tissue that is vascularized and functional. Applicants argue that Turischev teach the formation of a scar and that scar tissue is not vascularized or functional.

Applicants argue that the prior art was originally published in Russian.

Applicants argue that the claims have been amended to recite 'consisting essentially of'.

Applicant's arguments filed 11/18/10 have been fully considered but they are not persuasive.

Although Applicants argue (pages 8-9) that the claims recite wound repair and regeneration which refer to new tissue that is vascularized and functional and argue that Turischev teach the formation of a scar and that scar tissue is not vascularized or functional, it is first noted that the active step as claimed is administration. Turischev teach the effect of thymosin on the healing of flat skin wounds in rats (title). Turischev teach that Thymosin (5^{th} fraction) was used in the experiments (page 1 last paragraph). Turischev teach that the composition was administered intraperitoneally or topically to rats with wounds (page 2). Thus Turischev teach the active step and the agent as claimed. Since Turischev teach the elected agent (i.e. thymosin beta 4) which is recited in the claims (claim 188 for example) the claim limitations are met (see also MPEP 2112.01). Further, since Turischev expressly teach rats with skin wounds the patient population is met. In other words a subject with a wound is a subject in need of wound repair and regeneration. Applicants own claims 202-203 are evidence of the claim breadth. Turischev recognize the regenerative process in healing (page 1 first sentence, page 2 line 16, page 3 line 2, page 5 line 5). Turischev recognize the repair process in healing (page 1 3rd sentence, page 4 line 2). Although applicants make unsupported assertions about new functional tissue, such wording is not recited in the instant claims. The teachings of Turischev relating to a scar do not discredit the fact that Turischev teach the elected agent and elected patient population. It is contradictory to argue that the claims read on the elected species yet

argue that art that reads on the species is not applicable. As noted in the previous office action, the dictionary (The Free online dictionary (entry for healing) http://www.thefreedictionary.com/healing accessed on 5/26/10 4 pages) expressly defines healing to be repair (page 1, heal 2nd definition). Applicants assertion is contradictory to the term definition.

Although Applicants argue that the prior art was originally published in Russian, there is no requirement that prior art must originally be published in the English language. In accord with MPEP 706.02 II a translation has been provided for the applicant. Section 2121 of the MPEP expressly states that prior art is presumed to be enabled (regardless of the original publication language).

Although Applicants argue that the claims have been amended to recite 'consisting essentially of', it is noted that the claims also recite the open language 'containing' and claims 198,210,212,215,217 are evidence that there can be other components in the mixture. Further, the claims recite the open language 'comprises LKKTET'. MPEP 2111.03 states: 'For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising."'. In the instant case the specification provides no specific information of the basic and novel characteristics thus the term is construed as equivalent to comprising.

Claim Rejections - 35 USC § 103

Claims were previously rejected based on Turischev (Farmatsiya 'Examining the effects of thymosin on the healing of flat cutaneous wounds in rats' v45 (1996) pages 42-43; first cited 12/30/09) and Mann (US 6,030,948) and Puolakkainen et al (Journal of Surgical Research v58 1995 pages 321-329 first cited 4/29/09). Since the claims have been amended the rejection is updated to correspond to the instant claims.

Claims 187-188,191-196,198-200,202-205,208-213,215-217,219-221,223 are rejected under 35 U.S.C. 103(a) as being unpatentable over Turischev (Farmatsiya 'Examining the effects of thymosin on the healing of flat cutaneous wounds in rats' v45 (1996) pages 42-43; first cited 12/30/09) and Mann (US 6,030,948) and Puolakkainen et al (Journal of Surgical Research v58 1995 pages 321-329 first cited 4/29/09).

It is noted that Turischev is in a non-English language. A translated version of the article has been provided and will be relied upon and referenced to herein (Turischev translation of Farmatsiya 'Examining the effects of thymosin on the healing of flat cutaneous wounds in rats' total of 7 pages including the cover page)

Turischev teach the effect of thymosin on the healing of flat skin wounds in rats (title). Turischev teach that Thymosin (5^{th} fraction) was used in the experiments (page 1 last paragraph). Turischev teach that the composition was administered intraperitoneally or topically to rats with wounds (page 2). Turischev teach that there is clear acceleration of the healing rates and that a dose of 0.8 ug accelerated wound healing (page 3). Turischev does not recite the components of thymosin 5^{th} fraction. Mann teach (column 4 lines 8-53) that thymosin fraction 5 contains

thymosin beta4 (column 4 line 31) and thymosin alpha 1 (column 4 line 26). Mann is cited as a universal fact to reveal the components of thymosin fraction 5 and thus need not be prior art (MPEP 2124).

Turischev does not expressly teach transforming growth factor beta as recited in claims 198-199,215-216,231-232. Turischev does not expressly teach recombinant or synthetic polypeptides as in claims 191 and 208. Turischev does not expressly teach sterile water as a carrier as recited in claims 194,211.

Turischev teach the effect of thymosin on the healing of flat skin wounds in rats (title). Turischev teach that Thymosin (5^{th} fraction) was used in the experiments (page 1 last paragraph). Turischev teach that the composition was administered intraperitoneally or topically to rats with wounds (page 2). Turischev teach that there is clear acceleration of the healing rates and that a dose of 0.8 ug accelerated wound healing (page 3). Turischev does not recite the components of thymosin 5^{th} fraction. Mann teach (column 4 lines 8-53) that thymosin fraction 5 contains thymosin beta4 (column 4 line 31) and thymosin alpha 1 (column 4 line 26). Mann is cited as a universal fact to reveal the components of thymosin fraction 5 and thus need not be prior art (MPEP 2124). Since Turischev teach rats with skin wounds the patient population of claims 187,202,203 (i.e. skin damage),204,219,220 (i.e. epidermal),221,223 (skin damage) are met. Since Turischev teach that the composition was administered intraperitoneally or topically via a solution (page 2) the limitations of claims 192-193,195,196,209,210,212,213 are met. Turischev teach that Thymosin (5^{th} fraction) was used in the experiments (page 1 last paragraph) and Mann states that such fraction contains thymosin beta 4 and thymosin alpha 1 (see applicants original

claim 12 and admission on page 21 lines 4-5 of the reply dated 3/30/10, and see page 11 of specification of the current invention) the composition limitations of claims 187,188,200,204,205,217 are met.

Turischev teach that the composition was administered via a solution (page 2). One would recognize water as a common component of a solution. Since the experiments are carried out on live mammals one would want to ensure that there is no unnecessary contamination and thus one would be motivated to use sterile water. Since Turischev expressly teach positive results (there is clear acceleration of the healing rates and that a dose of 0.8 ug accelerated wound healing (page 3)) one would be motivated to carry out the methods of Turischev. Since water is a common component of a solution one would be motivated to use such component thus meeting the limitation recited in claims 194,211. In other words, in order to use the TB4 for skin wounds one would be motivated to prepare the TB4 with an appropriate excipient such as water and an appropriate form such as a lotion for administration to the skin. One would have a reasonable expectation of success since Turischev expressly teach positive results (there is clear acceleration of the healing rates and that a dose of 0.8 ug accelerated wound healing (page 3)).

Like Turischev, Puolakkainen also teach experiments that test methods of wound healing in rats (abstract). Puolakkainen recognize what is well-known in the art, that TGF-beta is known to enhance wound healing (title, page 325 discussion). In fact, Puolakkainen teach that TGF-beta significantly enhanced wound healing (abstract). One would be motivated to use the teachings of Puolakkainen along with Turischev since the references are drawn to methods of wound healing. The ides of combining them logically flows from their having been individually aught in the art. As such, one would be motivated to administer both thymosin beta 4, TGF-beta thus meeting the

limitations as recited in claims 198-199,215-216. Further, Puolakkainen recognizes (page 322 section preparation of the TGF-beta) using recombinant forms of the proteins. One would be motivated to also use recombinant forms of the other proteins thus meeting the limitations recited in claims 191 and 208.

In the instant case, the claimed elements (thymosin beta 4, TGF-beta) were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Taken together the references meet the limitations of the instant claims. One would have a reasonable expectation of success since both references teach agents for wound healing.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

It is noted that certain claims recite properties – actin-sequestering activity, stimulates epithelial migration, etc. Since Turischev teach the elected agent (i.e. thymosin beta 4) which is recited in the claims (claim 188 for example) the claim limitations are met (see also MPEP 2112.01). It is noted that the claims refer to effective amounts. Since Turischev expressly states (page 3) 'this is evidence of a clear acceleration of the healing rates' and 'a dose of 0.8 ug accelerated wound healing' the amounts are effective.

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting regeneration (claim 187) do not result in a manipulative difference and do not serve to limit the claims.

It is noted that claim 187 and claim 204 recite 'consisting essentially of'. First, it is noted that the claims also recite the open language 'containing' and claims 198,210,212,215,217 are evidence that there can be other components in the mixture. Further, MPEP 2111.03 states: 'For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising."'. In the instant case the specification provides no specific information of the basic and novel characteristics thus the term is construed as equivalent to comprising.

Claims were previously rejected based on Malinda et al (Faseb Journal 1997 cited in IDS 5/25/01) and Baumann et al 1997 (from 'Thymic peptides in preclinical and clinical medicine: an update:proceedings of the 2nd international thymus symposium' editor HR Maurer, pages 13-17) and Biotech Patent News (Dec 1 1997 1 page). Since the claims have been amended the rejection is updated to correspond to the instant claims.

Claims 187-188,191-196,200,202-205,208-213,217,219-221,223 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malinda et al (Faseb Journal 1997 cited in IDS 5/25/01) and Baumann et al 1997 (from 'Thymic peptides in preclinical and clinical medicine: an

update:proceedings of the 2nd international thymus symposium' editor HR Maurer, pages 13-17) and Biotech Patent News (Dec 1 1997 1 page).

Malinda teach that Thymosin beta 4 (TB4) acts as a chemoattractant for endothelial cells (abstract). Malinda teach that in vitro wound closure is more rapid in the presence of TB4 (page 477). Malinda teach that cell migration is enhanced by TB4 (page 478). Malinda teach that TB4 is important in angiogenesis and that the formation of blood vessels is an important part of wound healing (page 480). Malinda teach that others report that TB4 could play a major role in would healing (page 480).

Malinda does not expressly teach administration of TB4 to patients in need of wound repair.

Malinda teach that TB4 is important in angiogenesis and that the formation of blood vessels is an important part of wound healing (page 480). Malinda teach that others report that TB4 could play a major role in would healing (page 480). Malinda recognizes the use of in vivo experiments (abstract). Since Malinda teach positive results for the in vitro studies (see wound closure model page 477) one would be motivated to use the method in vivo.

Further, Baumann (Table II page 21) also teach that TB4 leads to an increase in wound healing in vitro.

Further, Biotech Patent News teach that investigators will use thymosin beta 4 (last paragraph) in a wound healing study.

Taken together, the prior art clearly recognizes the use of TB4 for wound healing. Although the references do not expressly teach in a single embodiment the use for patients in

need thereof one would be motivated to use TB4 in patients based on the promising in vitro results. One would have a reasonable expectation of success based on the in vitro results reported in the prior art.

Since Biotech patent news teach the use in wound healing studies one would be motivated to use TB4 specifically for those with wounds. Since Malinda teach the use of a scratch wound closure assay (page 475) one would be motivated to use TB4 in vivo for skin wounds. In order to use the TB4 for skin wounds one would be motivated to prepare the TB4 with an appropriate excipient such as water (in particular sterile water to prevent contamination) and an appropriate form such as a lotion for administration to the skin. Since in vitro models are used as a precursor to use in humans one would be motivated to use the methods on humans and apply TB4 to skin cells including epithelial cells (see page 474 of Malinda) based on the promising in vitro results. Although Malinda does not recite the source of the protein one would recognize that recombinant or synthetic production is a well known method in the art for production of peptides. Thus taken together the references obviate the use of a specific agent (thymosin beta 4) which reads on the polypeptide as recited in the instant claims; the references motivate a specific use (wound healing) which motivates specific excipients, forms, and locations of administration as recited in the instant claims.

Further, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g.doses), because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine

experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See MPEP § 2144.05). Thus, taken together the limitations of claims 187-188,191-196,200,202-205,208-213,217,219-221,223 rendered obvious based on the prior art.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

It is noted that certain claims recite properties – actin-sequestering activity, stimulates epithelial migration, etc. Since Malinda teach the elected agent (i.e. thymosin beta 4) which is recited in the claims (claim 188 for example) the claim limitations are met (see also MPEP 2112.01).

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting regeneration (claim 187) do not result in a manipulative difference and do not serve to limit the claims.

It is noted that claim 187 and claim 204 recite 'consisting essentially of'. First, it is noted that the claims also recite the open language 'containing' and claims 198,210,212,215,217 are evidence that there can be other components in the mixture. Further, MPEP 2111.03 states: 'For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear

indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising."'. In the instant case the specification provides no specific information of the basic and novel characteristics thus the term is construed as equivalent to comprising.

Claims were previously rejected based on Malinda et al (Faseb Journal 1997 cited in IDS 5/25/01) and Baumann et al 1997 (from 'Thymic peptides in preclinical and clinical medicine: an update:proceedings of the 2nd international thymus symposium' editor HR Maurer, pages 13-17) and Biotech Patent News (Dec 1 1997 1 page) and Puolakkainen et al (Journal of Surgical Research v58 1995 pages 321-329). Since the claims have been amended the rejection is updated to correspond to the instant claims.

Claims 187-188,191-196,198-200,202-205,208-213,215-217,219-221,223 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malinda et al (Faseb Journal 1997 cited in IDS 5/25/01) and Baumann et al 1997 (from 'Thymic peptides in preclinical and clinical medicine: an update:proceedings of the 2nd international thymus symposium' editor HR Maurer, pages 13-17) and Biotech Patent News (Dec 1 1997 1 page) and Puolakkainen et al (Journal of Surgical Research v58 1995 pages 321-329).

As discussed above, Malinda, Baumann, and Biotech Patent News teach the use of TB4 for wound healing and render obvious claims 187-188,191-196,200,202-205,208-213,217,219-221,223.

However, the references do not expressly teach in a single embodiment the use of a further agent or the use of TGF-beta as in claims 198-199,215-216.

Puolakkainen recognize what is well-known in the art, that TGF-beta is known to enhance wound healing (title, page 325 discussion). Puolakkainen also recognize the optimization of the administration mode and dose and teach toward topical administration (abstract and throughout). One would be motivated to use the teachings of Puolakkainen along with the other references since the references are drawn to methods of wound healing.

In the instant case, the claimed elements (thymosin beta 4, TGF-beta) were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Taken together the references meet the limitations of the instant claims. One would have a reasonable expectation of success since both references teach agents for wound healing. Taken together the references render obvious claims 187-188,191-196,198-200,202-205,208-213,215-217,219-221,223.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

It is noted that certain claims recite properties – actin-sequestering activity, stimulates epithelial migration, etc. Since Malinda teach the elected agent (i.e. thymosin beta 4) which is

recited in the claims (claim 188 for example) the claim limitations are met (see also MPEP 2112.01).

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting regeneration (claim 187) do not result in a manipulative difference and do not serve to limit the claims.

It is noted that claim 187 and claim 204 recite 'consisting essentially of'. First, it is noted that the claims also recite the open language 'containing' and claims 198,210,212,215,217 are evidence that there can be other components in the mixture. Further, MPEP 2111.03 states: 'For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising."'. In the instant case the specification provides no specific information of the basic and novel characteristics thus the term is construed as equivalent to comprising.

Response to Arguments 103

Applicants argue (pages 12-15) that Turischev does not teach that thymosin beta 4 or even thymosin fraction 5 has any effect such as claimed.

Applicants argue that Biotech Patent News is not peer-reviewed and talks about future studies.

Applicants argue that Malinda does not teach in vivo experiments and one would not have a reasonable expectation of success.

Applicant's arguments filed 11/18/10 have been fully considered but they are not persuasive.

Although Applicants argue (pages 12-15) that Turischev does not teach that thymosin beta 4 or even thymosin fraction 5 has any effect such as claimed, the facts clearly show that Turischev teach that there is clear acceleration of the healing rates and that a dose of 0.8 ug accelerated wound healing (page 3). Turischev recognize the regenerative process in healing (page 1 first sentence, page 2 line 16, page 3 line 2, page 5 line 5). Turischev recognize the repair process in healing (page 1 3rd sentence, page 4 line 2).

Although Applicants argue that Biotech Patent News is not peer-reviewed and talks about future studies, such statement is an unsubstantiated assertion. Further, there is no requirement that prior art must be peer reviewed. Further, talking about future studies is a clear suggestion to carry out such studies. In fact MPEP 2141 states that an exemplary rationale to support a conclusion of obviousness includes 'Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.'.

Although Applicants argue that Malinda does not teach in vivo experiments and one would not have a reasonable expectation of success, in the instant case, Malinda teach that TB4 is important in angiogenesis and that the formation of blood vessels is an important part of

wound healing (page 480). Malinda teach that others report that TB4 could play a major role in would healing (page 480). Malinda recognizes the use of in vivo experiments (abstract). Since Malinda teach positive results for the in vitro studies (see wound closure model page 477) one would be motivated to use the method in vivo. Further, Baumann (Table II page 21) also teach that TB4 leads to an increase in wound healing in vitro. Further, Biotech Patent News teach that investigators will use thymosin beta 4 (last paragraph) in a wound healing study. Taken together, the prior art clearly recognizes the use of TB4 for wound healing. Although the references do not expressly teach in a single embodiment the use for patients in need thereof one would be motivated to use TB4 in patients based on the promising in vitro results. One would have a reasonable expectation of success based on the in vitro results reported in the prior art and the suggestions of the prior art. Section 2145 of the MPEP states the arguments of counsel cannot take the place of evidence in the record. Prior art is presumed to be enabled (MPEP section 2121). Further, obviousness does not require absolute predictability (MPEP section 2143.02). Malinda expressly teach that in vitro wound closure is more rapid in the presence of TB4 (page 477), thus one would have a reasonable expectation of success.

Double Patenting

The double patenting rejections below are based on rejections from the previous office action. Since the claims have been updated the rejections have been updated to correspond to the instant claims.

The terminal disclaimer filed on 9/17/08 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US 7,268,118 has been reviewed and is accepted. The terminal disclaimer has been recorded.

The terminal disclaimer filed on 9/17/08 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on 11/284,430 has been reviewed and is accepted. The terminal disclaimer has been recorded.

It is noted that 10/714,405 has been abandoned.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 187-188,191-193,195-196,198-200,202-205,208-210,212-213,215-217,219-220,223 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 48-73 of copending Application No. 11/284,408

('408). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '408 application teaches methods of administering compositions to skin comprising thymosin beta four (for example, claim 48), transforming growth factor (claim 53), and a vehicle (claim 48) for topical treatment (for example, claim 52) in the form of a lotion (claim 72). '408 teach the administration to improve skin appearance and is applied to thinning skin (claim 53,70) and for wound repair (title) thus one would be motivated to administer to those of the instant claims. Taken together, the limitations of claims 187-188,191-193,195-196,198-200,202-205,208-210,212-213,215-217,219-220,223 are met.

It is noted that certain claims recite properties – actin-sequestering activity, stimulates epithelial migration, etc. Since '408 teach the elected agent (i.e. thymosin beta 4) which is recited in the claims (claim 188 for example) the claim limitations are met (see also MPEP 2112.01). It is noted that the claims refer to effective amounts. Since '408 expressly teach amounts (claim 48-49) and methods for improving the appearance of the skin (claim 53) the amounts are effective.

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting regeneration (claim 187) do not result in a manipulative difference and do not serve to limit the claims.

It is noted that claim 187 and claim 204 recite 'consisting essentially of'. First, it is noted that the claims also recite the open language 'containing' and claims 198,210,212,215,217 are

evidence that there can be other components in the mixture. Further, MPEP 2111.03 states: 'For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising."'. In the instant case the specification provides no specific information of the basic and novel characteristics thus the term is construed as equivalent to comprising.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 187-188,191-193,195-196,198,200,202-205,208-210,212-213,215,217,219-220,223 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 13-23,26 of copending Application No. 11/917,869 ('869). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '869 application teaches methods of administering compositions to the skin comprising thymosin beta four isoform or LKKTET (for example, claim 13,21), and a stimulating agent (claim 13), and a carrier (claim 17), and teach the composition as a lotion (claim 20), and teach specific doses (claim 23). The method is for treating tissue and injured or damaged skin thus one would be motivated to treat the patients as in the instant claims. Taken together, the limitations of claims 187-188,191-193,195-196,198,200,202-205,208-210,212-213,215,217,219-220,223 are met.

It is noted that certain claims recite properties – actin-sequestering activity, stimulates epithelial migration, etc. Since '869 teach the elected agent (i.e. thymosin beta 4) which is recited in the claims (claim 188 for example) the claim limitations are met (see also MPEP

2112.01). It is noted that the claims refer to effective amounts. Since '869 expressly teach amounts (claim 23) and methods for treating (claim 13) the amounts are effective.

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting regeneration (claim 187) do not result in a manipulative difference and do not serve to limit the claims.

It is noted that claim 187 and claim 204 recite 'consisting essentially of'. First, it is noted that the claims also recite the open language 'containing' and claims 198,210,212,215,217 are evidence that there can be other components in the mixture. Further, MPEP 2111.03 states: 'For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising."'. In the instant case the specification provides no specific information of the basic and novel characteristics thus the term is construed as equivalent to comprising.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 187-188,191-193,195-196,200,202-205,208-210,212-213,219-220,223 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-32 of copending Application No. 11/715,997 ('997). Although the conflicting claims are not identical, they are not patentably distinct from each other because the

'997 application teaches methods of administering compositions to the skin comprising thymosin beta four or LKKTET (for example, claim 21), and specific doses (claim 27), and as a lotion (claim 22), and with a carrier (claim 23). The method is for treating tissue and injured or damaged skin thus one would be motivated to treat the patients as in the instant claims. Taken together, the limitations of claims 187-188,191-193,195-196,200,202-205,208-210,212-213,219-220,223 are met.

It is noted that certain claims recite properties – actin-sequestering activity, stimulates epithelial migration, etc. Since '997 teach the elected agent (i.e. thymosin beta 4) which is recited in the claims (claim 188 for example) the claim limitations are met (see also MPEP 2112.01). It is noted that the claims refer to effective amounts. Since '997 expressly teach amounts (claim 28) and methods for treating (claim 21) the amounts are effective.

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting regeneration (claim 187) do not result in a manipulative difference and do not serve to limit the claims.

It is noted that claim 187 and claim 204 recite 'consisting essentially of'. First, it is noted that the claims also recite the open language 'containing' and claims 198,210,212,215,217 are evidence that there can be other components in the mixture. Further, MPEP 2111.03 states: 'For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are,

"consisting essentially of" will be construed as equivalent to "comprising."'. In the instant case the specification provides no specific information of the basic and novel characteristics thus the term is construed as equivalent to comprising.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 187-188,191-193,195-196,200,202-205,208-210,212-213,219-220,223 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 of copending Application No. 12/444,331 ('331). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '331 application teaches methods of administering compositions to the skin comprising thymosin beta four or LKKTET (for example, claim 1), and specific doses (claim 7), and lotions as a form (claim 11).The method is for treating tissue and injured or damaged skin thus one would be motivated to treat the patients as in the instant claims. Taken together, the limitations of claims 187-188,191-193,195-196,200,202-205,208-210,212-213,219-220,223 are met.

It is noted that claim 187 and claim 204 recite 'consisting essentially of'. First, it is noted that the claims also recite the open language 'containing' and claims 198,210,212,215,217 are evidence that there can be other components in the mixture. Further, MPEP 2111.03 states: 'For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising."'. In the instant case the specification provides no specific information of the basic and novel characteristics thus the term is construed as equivalent to comprising.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 11/715,997 and 12/444,331; discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Response to Arguments Double Patenting

Applicants state that claims have been rejected over claims in 3 separate pending patent applications.

Applicants request (page 16-17) that the rejections be held in abeyance.

Applicant's arguments filed 11/18/10 have been fully considered but they are not persuasive.

Although Applicants state that claims have been rejected over claims in 3 separate pending patent applications, there are 4 (11284408, 11917869, 11715997, 12444331) not 3 separate pending patent applications that are used in the rejections.

Although Applicants request that the rejections be held in abeyance, such request does not overcome the rejection. The instant claims are not allowable.

Prior art of record

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Bilton (WO 84/02274) - Bilton teach compositions for wound healing (title) including those that include thymus concentrate (claim 1, example 1).

Conclusion

Claims were previously rejected under 102,103,double patenting. As set forth above certain rejections are maintained and the rejections have been updated based on applicants claim amendments.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ronald T Niebauer/
Examiner, Art Unit 1654

/Cecilia Tsang/

Supervisory Patent Examiner, Art Unit 1654